April 15, 2003

Frederick R. Johannsen
Technical Contact
Solutia, Inc.
575 Maryille Centre Drive
St. Louis, MO 63141

Dear Mr. Johannsen:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for Hexanedioic Acid, Di-C7-C9 Branched and Linear Alkyl Ester posted on the ChemRTK HPV Challenge Program Web site on December 16, 2002. I commend Solutia, Inc. for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that Solutia, Inc. advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

-S-

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: C. Auer
A. Abramson
W. Penberthy
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
Hexanedioic Acid, Di-C7-C9 Branched and Linear Alkyl Ester (97 Adipate)

Summary of EPA Comments

The sponsor, Solutia, Inc., submitted a test plan and robust summaries to EPA for Hexanedioic acid, di-C7-C9 branched and linear alkyl ester (97 Adipate, CAS No. 68515-75-3) dated November 19, 2002. EPA posted the submission on the ChemRTK HPV Challenge Web site on December 16, 2002. Information was also included for two non-sponsored compounds: di(n-hexyl) adipate (CAS No. 9110-33-8) and dioctyl adipate (CAS No. 103-23-1).

EPA has reviewed this submission and has reached the following conclusions:

1. Physicochemical Properties. EPA agrees that testing is not necessary for melting point, water solubility, and partition coefficient. The submitter needs to measure vapor pressure at ambient temperature or explain why the compound had to be tested at 224°C and also provide details on the boiling point experiment to determine whether it is adequate.

2. Environmental Fate. EPA agrees that testing is not necessary for stability in water. The submitter needs to provide estimated data for indirect photolysis in the atmosphere. Biodegradation testing is also needed as the submitted data do not address the SIDS ready biodegradation endpoint.

3. Health Effects. All appropriate SIDS-level endpoints have been addressed for the purposes of the HPV Challenge Program. However, a missing summary for one genetic toxicity study needs to be added and some deficiencies in submitted summaries need to be addressed.

4. Ecological Effects. The submitter proposed no additional ecotoxicity testing. However, the results for acute toxicity testing in fish, daphnia, and green algae are not adequate because they were tested above the water solubility limit and the test concentrations were not measured. EPA suggests that a 21-day chronic reproductive study in daphnia be conducted in accordance with guidance on chemicals that have log Kow values equal to or greater than 4.2.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA Comments on the Hexanedioic Acid, Di-C7-C9 Branched and Linear Alkyl Ester Challenge Submission

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

EPA agrees with the submitter that adequate data are available for melting point, water solubility, and partition coefficient (log K_{ow}) for purposes of the HPV Challenge Program.

Melting Point. While 97 Adipate is a liquid at room temperature, according to OECD TG 102 measured data need to be provided unless the melting point is less than 0°C. EPA located an experimental melting point of –79 °C for the analog dioctyladipate (CAS No. 103-23-1) (Verschueren, 2001). Since this indicates an expected melting point below the threshold, the data appear sufficient for this endpoint. The submitter needs to include the measured melting point information for dioctyladipate in the test plan and robust summary.

Boiling Point. The submitter needs to clarify the boiling point data. The submitter provided a measured boiling point of 224°C for the title substance. EPA needs more information on this study and reserves judgment on this endpoint pending receipt of that information (see below).

Vapor Pressure. Vapor pressure at ambient temperature should be measured according to OECD TG 104 as the submitter has provided data determined at elevated temperature (224°C). According to OECD TG 104, vapor pressure studies should be conducted at 20 or 25 °C. Estimated values showing a compound to have a vapor pressure less than $1x10^{-5}$ Pa ($7.5x10^{-8}$ mm Hg) at 25 °C are acceptable if measured data are not available. However, estimated values for the test substance and the analogs di(n-hexyl)adipate and dioctyladipate were 6.1 x 10^{-5}, $2.88x10^{-6}$ and $8.5x10^{-7}$ mm Hg, respectively (SRC, 2000). Since the estimated values of the title substance and its analogs exceed the OECD TG 104 criterion, measured data are needed.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity).

EPA agrees with the submitter that adequate data are available for stability in water and fugacity for the purposes of the HPV Challenge Program

Photodegradation. The information provided address photodegradation potential in water. The submitter needs to estimate indirect photooxidation half-lives for 97 Adipate in air using AOPWIN. In addition, the submitter should provide information on direct photodegradation, specifically whether the compound absorbs at > 290 nm.

Biodegradation. The submitter has provided data from an inherent test as well as a second screening study using an acclimated inoculum. While the submitter states that data from these two tests indicate the ready biodegradability of the test substance, neither of these tests measures ready biodegradation. Therefore, a ready test should be conducted according to OECD guidelines to provide data suitable for this endpoint.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

All health effects endpoints have been adequately addressed for the purposes of the HPV Challenge Program and no additional testing is needed. However, the submitter needs to provide a missing robust summary for genetic toxicity and address a few deficiencies in existing robust summaries.

Repeated-Dose Toxicity. The sponsor needs to address an inconsistency between the high dose levels for the 90-day dietary assay as listed on page 12 of the test plan (1500 and 1900 mg/kg/day for males and females, respectively) and in the robust summary (1300 and 1800 mg/kg/day).

Genetic Toxicity. The negative bacterial mutagenicity test for the sponsored compound was adequate. Although the study only used four rather than five bacterial strains, this was adequate according to the then-current protocol (1981). The data from this study, in combination with data on the two analogs (dioctyl adipate and di(n-hexyl) adipate), satisfy the gene mutation endpoint. Data on chromosomal aberrations for the analog (di(n-hexyl) adipate) are adequate. However, a robust summary for the mouse lymphoma assay done with 97 Adipate (according to the second paragraph under Section 3, page 13 of the Test Plan) needs to be provided.

Reproductive Toxicity. EPA agrees with the submitter's proposal to address this endpoint with the combination of a developmental toxicity assay and the histopathological examination of reproductive organs in the repeated-dose toxicity study. However, the submitter needs to provide an explanation, in robust summary format, in the reproductive toxicity section that summarizes the assessment and results for male and female reproductive organs as mentioned on page 7 of the test plan.

Ecological Effects (fish, invertebrates, and algae).

EPA considers the acute test data in fish, daphnia, and algae for CAS No. 68515-75-3 inadequate because this chemical was tested above its water solubility and without measured concentrations. The submitter states that the measured Log Kow for 97 Adipate is 6.49. For chemicals with Log Kow values equal to or greater than 4.2 EPA recommends daphnia chronic testing using measured concentrations at or below the water solubility of 97 Adipate. Testing should also follow the *Guidance on Aquatic Toxicity Testing of Difficult Substances and Mixtures* on the OECD Web site at http://www.olis.oecd.org/olis/2000doc.nsf/LinkTo/env-jm-mono(2000)6.

Specific Comments on the Robust Summaries

Generic comments

Each summary should clearly identify the test substance by the chemical name. In many cases, the test material could be determined only by looking up the study title in the reference list and consulting the list of compound synonyms on page 4 of the test plan. The submitter should consult EPA guidance documents for the preparation of robust summaries (http://www.epa.gov/opptintr/chemrtk/guidocs.htm).

Physicochemical Properties

Boiling point. The summary lacks the pressure at which the experiment was conducted.

Environmental Fate

Stability in Water. The submitter has provided estimated values. The submitter needs to provide a discussion in robust summary format that focuses on the low water solubility, which makes the measurement of hydrolysis impractical (expanding on what was said on page 10 of the Test Plan).

Health Effects

Repeated-Dose Toxicity. The method section needs to be revised to more clearly specify that histologic examination by light microscopy was done (on “a complete set of approx. 40 tissues”) and to specify the reproductive organs that were microscopically examined.

Developmental Toxicity. The submitter needs to provide the incidence data by dose for the effects observed (decreases in maternal body weight and fetal body weight, and increase in rudimentary structures in fetuses).

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

References

SRC (2000). Syracuse Research Corporation, MPBPWIN v. 1.40, 2000.

Verschueren, K. (2001). Handbook of Environmental Data on Organic Chemicals, 4th edition, Vol 1: 975, John Wiley & Sones, Inc.: New York.